REMARKS

The Office Action and the cited and applied reference have been carefully studied. Claim 97 is allowed. Claims 93-96 and 98-119 are also pending and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

The specification has been objected to as failing to provide proper antecedant basis for the claimed subject matter.

The title of the invention is now amended to provide consistency with the titles of the invention in parent applications 08/502,535 and 08/908,005 (divisional of 08/502,535) as they appear in issued U.S. Patent nos. 5,912,324 and 5,914,253, respectively. Applicants submit that the terms "IGIF" or "IL-18" are new names given in the art to the "interferon-gamma inducing protein" according to the present invention. Applicants at first called the claimed protein "interferon-gamma inducing protein" based on its function because it was a novel protein that was unnamed at the time the present invention was made. Afterwards, during prosecution of the present application and its parent application no. 08/502,535, the "interferon-gamma inducing protein" became known at first by persons in the art as "IGIF" for interferon-gamma inducing factor and then as "IL-18". Thus, the interferon-gamma inducing protein for which the monoclonal antibody of the present invention specifically recognizes is also known as "IGIF" and "IL-18", which are simply

commonly used names for the same protein. Copies of U.S. Patent nos. 5,912,324 and 5,914,253 are attached hereto.

Reconsideration and withdrawal of this objection are therefore respectfully requested.

Claims 93-96, 100, 104, 107-110, and 113-118 have been rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The examiner states that applicants have not pointed out, nor can the examiner locate, the basis in the specification for the newly introduced recitation of "IGIF" and/or "IL-18" in these claims. This rejection is respectfully traversed.

As discussed above with respect to the objection to the specification, the terms "IGIF" and "IL-18" are simply different names used for the same protein, the IFN-γ inducing protein according to the present invention. Applicants submit that this is not new matter, as the examiner in charge of handling the related applications, which issued as U.S. Patent nos. 5,912,324 and 5,914,253, well recognized.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 93-118 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. This rejection is respectfully traversed.

This rejection as it relates to the recitation of IGIF and IL-18 is believed to be overcome by the amendments to claims 93 and 118 and the discussion above regarding the terms "IGIF" and "IL-18" as simply different art recognized names used for the IFN-γ inducing protein according to the present invention.

With regard to the language "substantially the same" in claim 93, applicants submit that this language is not indefinite. The Court of Appeals held in *Arnold Pipe Rentals Company, Inc. v Engineering Enterprises*, 146 USPQ 416, that absolute precision in wording of claims, while desirable, would be an unreasonable burden to impose on inventor and that descriptive words such as "substantial", "high", "about", and "slight excess" have often withstood attack under 35 U.S.C. 112; thus, "at least substantially flat" is not fatally indefinite. Attached hereto are copies of U.S. Patents 6,156,315 (issued within the past year) and 5,429,936, which accepted the use of the claim language "substantially the same."

The remaining indefiniteness issues are obviated by the amendments to the claims.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 93, 94, 96, 118, and dependent claims 95, 98-117 have been rejected under 35 U.S.C. 112, first paragraph, because the examiner states that the specification, while being enabling for claims limited in scope to a monoclonal antibody specifically recognizing a polypeptide of SEQ ID NO:2, wherein Xaa is Met or

Thr, does not reasonably provide enablement for claims to monoclonal antibodies against variants of SEQ ID NO:2 (as recited in claims 93, 94, 96), or any "interferon-γ inducing protein" (claim 118). This rejection is respectfully traversed.

At the time the claimed invention was made, it was possible for the skilled artisan to obtain variants of the polypeptide having an amino acid sequence of SEQ ID NO:2 (wherein Xaa is Met or Thr) and to prepare monoclonal antibodies specific to the variants. See U.S. Patent no. 5,304,496, a copy of which is attached. It is therefore believed that it would have been possible for the skilled artisan at the time the claimed invention was made to obtain the monoclonal antibody of the presently claimed invention without undue experimentation once the amino acid sequence of SEQ ID NO:2 is known.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 93-96 and 98-117 remain rejected, and claim 118 has been rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants submit that although the examiner states that to the extent the claims encompass antibodies that bind to epitopes not found in the particularly disclosed sequences, there is no written description of those epitopes, the examiner's

requirement is not a realistic one. It is impossible (even for the skilled person) to check if a monoclonal antibody to a certain polypeptide binds to any other polypeptide and disclose the results in the specification. In fact, applicants are aware of no patent specification issued in the United States and other countries that checks if a monoclonal antibody to a certain polypeptide binds to other polypeptides and then discloses the results. It is in fact impossible to check and confirm that a monoclonal antibody, which specifically binding to a particular polypeptide, does not bind to all other polypeptides.

When a skilled person intends to obtain a monoclonal antibody against a polypeptide X, the skilled person can easily obtain a monoclonal antibody which specifically binds to the polypeptide X without undue experimentation if the polypeptide X or its sequence is provided. The monoclonal antibody of the present invention is obtainable using a polypeptide having an amino acid sequence of SEQ ID NO:2 (Xaa is Met or Thr) disclosed in the specification and variants thereof. Accordingly, applicants believe that a monoclonal antibody of the present invention can be easily obtained by a skilled person based on the state of the art and with only routine experimentation.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 93-118 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Nakamura et al. (Infect. Immun. 61:64-70:1993). This rejection is respectfully traversed.

An "interferon-gamma (IFN-γ) inducing protein, (IGIF and IL-18)" of the present invention shows 19,000 ± 5,000 daltons on SDS-PAGE. By contrast, the factor of Nakamura shows a molecular weight of 50,000 - 55,000 (50-55 kDa) on SDS-PAGE (see page 66, right lower column and page 67, left upper column, Fig. 2). This difference is significant. The fact that the molecular weights measured with the same method are different means that the two substances are different.

The examiner states that if the factor of Nakamura is a polymer of an "interferon-gamma (IFN-γ) inducing protein, (also known as IGIF and IL-18)" of the present invention, then the difference can be explained. However, it should be noted that Nakamura never confirmed the presence of IGIF having a molecular weight of 19,000 ± 5,000 daltons by purification and separation.

Furthermore, Nakamura discloses at page 68, right column, second paragraph, that Nakamura's factor having a molecular weight of 50-55 kDa loses IFN-γ inducing activity after treatment on SDS-PAGE. By contrast, IGIF having a molecular weight of 19,000 ± 5,000 daltons maintains its IFN-γ inducing activity as disclosed in the present specification page 23, Experiment 2-1.

It is therefore believed that IGIF of the claimed invention and Nakamura's factor are clearly different based on the following points:

(a) molecular weight;

(b) there is no disclosure in Nakamura which suggests that Nakamura's factor is a polymer of the IGIF of the claimed invention and which discloses that a monomer is actually purified and separated; and

(c) Nakamura's factor loses its IFN-γ inducing activity when treated on SDS-PAGE.

Thus, Nakamura neither discloses nor suggests a monoclonal antibody against the IGIF of the present invention. It is therefore believed that the claimed invention is not obvious over Nakamura.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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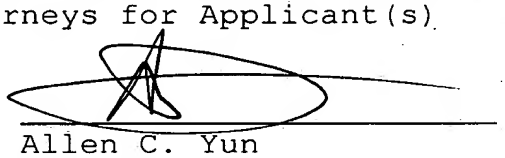
By: 
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"VERSION WITH MARKINGS TO SHOW CHANGES MADE"

IN THE SPECIFICATION

The paragraph under the CROSS-REFERENCE TO RELATED APPLICATIONS heading has been replaced with the following rewritten paragraph:

--This application is a continuation application of copending parent application no. 08/502,535, filed July 14, 1995, now issued as U.S. Patent no. 5,912,324.

IN THE CLAIMS

Claims 93-95 and 118 have been amended as follows:

93(Once-amended). A monoclonal antibody which specifically recognizes (i) an interferon-gamma (IFN-γ) inducing protein ~~(IGIF, IL-18)~~, also known as IGIF and IL-18, having the following physiochemical properties or (ii) a variant thereof which has substantially the same physicochemical properties as the protein of (i) ~~and~~ but has an amino acid sequence of SEQ ID NO:2~~, wherein~~ in which one or more amino acids are replaced with different amino acids, one or more amino acids are added to the N- or C-terminus of SEQ ID NO:2, or one or more amino acids at the N- or C-terminus of SEQ ID NO:2 are deleted:

(1) Molecular weight

19,000 ± 5,000 daltons on gel filtration and sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE);

(2) Isoelectric point (pI)

4.8 ± 1.0 on chromatofocusing;

(3) Biological activity

Inducing the interferon-γ production by immunocompetent cells; and

(4) Partial amino acid sequence

Possessing a part of the whole of the amino acid sequence of SEQ ID NO:2, wherein Xaa is Met or Thr.

94(Once-amended). A monoclonal antibody according to claim 93, wherein the amino acid sequence of the IGIF or IL-18 is encoded by a cDNA which ~~is hybridizable~~ hybridizes with a probe having the coding sequence shown in SEQ ID NO:1 at 60°C in a solution of 5 x SSPE, 5 x Denhardt's solution, 0.5% (w/v) sodium dodecyl sulfate (SDS), and 100 µg/ml denatured salmon sperm DNA and after washing in 6xSSC.

95(Once-amended). A monoclonal antibody according to claim 93, wherein said IGIF or IL-18 is obtainable from ~~mice~~ a mammal.

118(Once-amended). A monoclonal antibody specific to interferon-gamma (IFN-γ) inducing protein, also known as IGIF and IL-18 ~~(IGIF, IL-18)~~.